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LEADING ARTICLE

The Role of Patient-Reported Outcomes to Measure Treatment Satisfaction in Drug Development

Carolina Navas[1] · Alexandra Palmer Minton[2] · Ana Maria Rodriguez-Leboeuf[1]

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Abstract

Treatment satisfaction is a person's rating of his or her treatment experience, including processes and outcomes. It is directly related to treatment adherence, which may be predictive of treatment effectiveness in clinical and real-world research. Consequently, patient-reported outcome (PRO) instruments have been developed to incorporate patient experience throughout various stages of drug development and routine care. PRO instruments enable clinicians and researchers to evaluate and compare treatment satisfaction data in different clinical settings. It is important to select fit-for-purpose PRO instruments that have demonstrated adequate levels of reliability, validity, and sensitivity to change to support their use. Some of these instruments are unidimensional while some are multidimensional; some are generic and can be applied across different therapeutic areas, while others have been developed for use in a specific treatment modality or condition. This article describes the role of treatment satisfaction in drug development as well as regulatory and Health Technology Assessment (HTA) decision making and calls for more widespread use of carefully selected treatment satisfaction PRO instruments in early- and late-phase drug development.

Key Points for Decision Makers

This paper provides an overview of the role of treatment satisfaction in drug development, regulatory and HTA decision making.

The main goal is to call for more extensive use of fit-for-purpose PRO instruments to assess treatment satisfaction in all phases of drug development.

1 Introduction

In the era of patient-centered drug development, it is critical for drug developers, regulators, payers, and researchers to collect and understand the patients' perspectives on drugs (and other treatments) during their development [1, 2]. When a treatment is approved and made available for clinical use, data on how patients feel whilst taking the treatment provides healthcare professionals and patients with valuable insights, enabling the delivery of evidence-based medicine. Evidence-based medicine refers to the application of the best available research to clinical care, which requires the integration of evidence with clinical expertise and patient values [3]. The measurement of treatment satisfaction using a PRO instrument offers a standardized way of generating such data during treatment development.

2 Treatment Satisfaction Definition

Treatment satisfaction is defined as the individual's rating of important attributes of the process and outcomes of their treatment experience [4, 5]. An individual's satisfaction with a treatment will be influenced by their knowledge and experience of the treatment. Specifically, perceived or experienced treatment effectiveness, administration complexity and convenience, discomfort and side effects (see the Decisional Balance Model of Treatment Satisfaction [6]; Fig. 1a), as well as cost of the treatment will inform how satisfied or dissatisfied an individual is with a treatment [7]. Patient expectations, demographic characteristics (age and education), and personal preferences can also affect treatment

✉ Carolina Navas
carolina.navas@iqvia.com

1 IQVIA, Patient-Centered Solutions, Madrid, Spain

2 IQVIA, Patient Centered Solutions, Boston, MA, USA

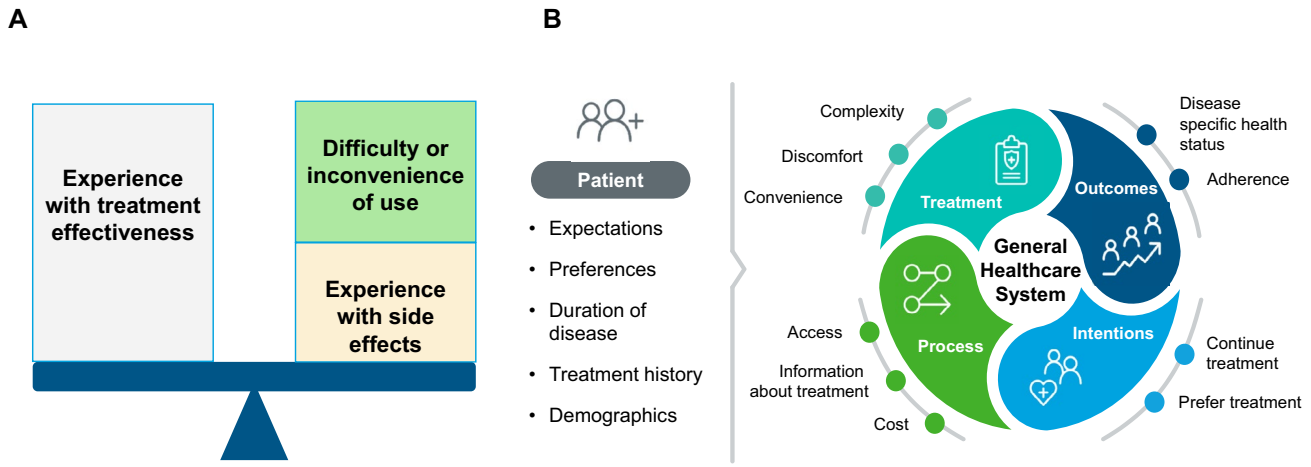

Fig. 1 Treatment satisfaction framework: **a** Decision balance model of treatment satisfaction. **b** Adaptation of Weaver and colleagues' conceptual model of treatment satisfaction [9]

satisfaction, as can prior experience with disease and with treatment [8].

Treatment satisfaction can be a useful concept for researchers, intervention developers, and healthcare professionals wishing to understand the patient experience with treatment, and to differentiate among alternative treatments. Understanding treatment satisfaction can also help with understanding the likelihood of adherence and persistence to treatment [4]. This can ultimately lead to improved health status as depicted in the conceptual framework of treatment satisfaction developed by Weaver and colleagues [9] (Fig. 1b).

The association between treatment satisfaction, adherence, and persistence is clinically intuitive. If a patient is not satisfied with treatment, this feeling may negatively affect his or her behavior in terms of regimen execution as well as his or her willingness to persist with the treatment [6]. The connection between treatment satisfaction and persistence is even more important in chronic diseases where up to one half of patients make medication-related decisions without seeking medical advice [10]. Indeed, in chronic diseases, patient dissatisfaction (rather than clinical consultation and decision making) is one of the main drivers of treatment discontinuation [6, 11–13], which in turn can lead to an increased rate of complications, deterioration in health, and ultimately death [6, 14, 15].

Understanding treatment satisfaction across multiple treatments can also help to predict patient preferences for alternative treatments—an important consideration when there are several options for treatment that involve alternate routes of administration, types of medication, or drug regimens [16] [17]. Research in oncology has shown, for instance, that treatment satisfaction and adherence are highest when people are offered treatment that is in line with their own preferences [18].

3 Treatment Satisfaction Measurement

Treatment satisfaction is a highly individual and personal experience. To understand this concept, researchers as well as healthcare providers must rely on patients' reports [4]. Patient reports can be generated in two ways: through narrative exploration (i.e., by talking to patients to qualitatively understand their experiences) or through PRO instruments (i.e., using standardized questionnaires to generate quantitative data).

Qualitative research offers the opportunity to explore satisfaction in depth, including drivers of satisfaction and implications of being satisfied/dissatisfied in terms of feelings and behaviors. Qualitative research can, however, be intrusive; reactive to personalities, moods and interpersonal dynamics between interviewer and interviewee; expensive; and time consuming [19].

PRO instruments are measures of a patient's perspective as reported directly from the patient without added interpretation by a healthcare worker or anyone else [20]. PRO instruments offer a way to collect patient information quickly and in a standardized manner and are thus frequently used to evaluate the impact of disease and treatments on the patient's functioning, well-being, and everyday life in clinical trials [4].

There are a large number of PRO instruments measuring treatment satisfaction [21]. They differ on a number of parameters, including number of items, measurement properties, and targeted use.

3.1 Number of Items

Some treatment satisfaction PRO instruments consist of a single item measuring global treatment satisfaction [22]. Other intruments include multiple items, some of which may contribute to one overall rating of satisfaction, or they may measure different dimensions of satisfaction (efficacy, side effects, convenience) [23]. Single-item measures offer simplicity and speed. However, use of a single item can mean the loss of important information about how patients view a treatment. Most of the patients that answer single-item questionnaires, for example, report high levels of satisfaction regardless of other negative information [24].

3.2 Measurement Properties

PRO instruments need to demonstrate that they measure what they were designed to measure in a reliable, valid, and an interpretable way in order to be considered 'fit for purpose' to support regulatory, payer, and healthcare decision making. A 'fit for purpose' PRO instrument demonstrates the following measurement properties: reliability (internal consistency and test re-test), validity (content and construct), and responsiveness (sensitivity to change) [25]. Sound measurement properties are not just critical for PRO instruments but rather applicable to all measurement methodologies for data collection [26]. Without evidence of reliability, validity, and sensitivity to change, the PRO instrument may produce inconsistent results that cannot be replicated or compared across studies, leading to inaccurate or misleading study results and a risk of misattribution of outcomes to the treatment under investigation [26].

3.3 Targeted Use

Treatment satisfaction PRO instruments can be generic (i.e., designed for use across different disease/therapeutic populations) or disease/context-specific (i.e., built to address those aspects of satisfaction that are important for a particular and specific group of patients) [27] [28]. Generic instruments allow for comparisons between diseases, across different populations, or across medication types and patient conditions [29]. Whereas disease/context-specific instruments arguably possess greater potential for showing differences between competing therapies, they cannot be applied across populations [30]. Examples of generic and disease-specific questionnaires developed for use in routine care and drug development to assess treatment satisfaction from patients are presented in Tables 1 and 2, respectively [31–48].

4 Treatment Satisfaction in Drug Development

The measurement of treatment satisfaction should not be prioritized over efficacy, safety, or survival data (which have been frequently used as primary indicators for drug development [52]). However, as barriers to developing new products increase, and the number of markets with generic competition or at least multiple alternative treatments grow, satisfaction can be an important secondary endpoint to provide information about how people feel about the treatment they took in the trial and provide evidence of the value (or concerns) of certain treatments. This can support key efficacy, safety, and survival endpoints [53].

Thus, treatment satisfaction has become an important outcome for drug development [54], particularly in trials (1) comparing treatments that present differences in terms of efficacy or side effects; (2) comparing treatments that are similar in terms of efficacy but have different routes of administration or dosing schedules; or (3) where demonstration of satisfaction with a medication relative to a comparator is considered to indicate adherence benefits [16] and/or treatment effectiveness [55]. Generic and disease-specific, multidimensional, and single-item PRO instruments can be useful to measure treatment satisfaction in clinical trials for novel drugs in development. But to do so, they must have demonstrated evidence of reliability, validity, and responsiveness for the intended use.

The use of PRO treatment satisfaction instruments in clinical research has increased in recent years, in line with various initiatives focusing on increasing the patient perspective in drug development [56]. From the authors' recently completed review of *clinicaltrials.gov* data, it was found that 4978 clinical studies assessed a treatment satisfaction endpoint between 2004 and 2015, and 8488 clinical studies assessed a treatment satisfaction endpoint between 2016 and 2023 (data on file). The evaluation of treatment satisfaction as an outcome in drug development, however, only represents a small fraction of the total studies undertaken during this time (3.3%). The recent development of clear guidelines from regulators for the use of PRO instruments to support clinical trial evidence (e.g., the FDA Patient-Focused Drug Development [PFDD] [20] guidance), an increased concern towards patient centricity throughout the product evidence lifecycle, and an increase in the development of drugs that differentiate through non-efficacy parameters (e.g., by frequency or modality of administration, side-effect profiles, etc.) suggests that treatment satisfaction endpoints in clinical trials are likely to increase in coming years.

Table 1 Examples of generic treatment satisfaction patient-reported outcome (PRO) instruments

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Treatment Satisfaction with Medicines Questionnaire (SATMED-Q) [31, 32]	Measure patient satisfaction with chronic diseases (T2DM, arterial hypertension, arthrosis, BPH, COPD/asthma, depression, and migraine) subjected to any type of prolonged pharmacological treatment	Adult	The past month	17	Treatment effectiveness (3 items) Convenience of use (3 items) Impact on daily activities (3 items) Medical care (2 items) Undesirable side effects (3 items) Global satisfaction (3 items)	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient* Treatment effectiveness: 0.813; Convenience of use 0.861; Impact on daily activities 0.851; Medical care 0.885; Undesirable side effects 0.912; Global satisfaction 0.855 *Test-retest reliability (reproducibility)* Pearson correlation coefficient: 0.945 and Intra-class Correlation Coefficient (ICC): 0.943 **Validity:** *Clinical validity* The assessments of the clinicians were used to establish four groups of effectiveness (poor, acceptable, good, excellent). The groups of effectiveness formed with the assessments of the clinicians differ in the total composite score and for all the subscales ($p < 0.0005$ in all cases) except Convenience ($p = 0.315$) and Undesirable side effects ($p = 0.220$)

Table 1 (continued)

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Treatment Satisfaction Questionnaire for Medication TSQM-1.4 [6]	To measure patients' satisfaction with medication in chronic diseases such as coronary diseases [27], cystic fibrosis [35], hypertension [36], COPD [37], multiple sclerosis [38], diabetes [39], and autoimmune diseases such as psoriasis [40] and angiodema [41]	Adult	2–3 weeks, or since the last medication use	14	Side effects (5 items) Effectiveness (3 items) Convenience (3 items) Global satisfaction (3 items)	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient* Patients with arthritis, asthma, major depression, T1DM, high cholesterol, hypertension, migraine, $n = 280$ Effectiveness: 0.88; Side effects: 0.88; Convenience: 0.90; Global satisfaction: 0.86 **Validity:** *Clinical validity* Comparisons of mean side effects scores and mean effectiveness scores between individuals on medication for < 2 months and individuals on medication for a longer period. Mean effectiveness scores were ($F(df) = 8.57$, $p = 0.004$) lower in the < 2-months group (68.3 ± 18.8) than the longer period group (74.4 ± 17.2). Mean side effects scores were significantly ($F(df) = 4.76$, $p = 0.03$) lower in the < 2-months group (84.6 ± 16.4) than the longer period group (88.4 ± 14.2) *Known-groups validity* Comparisons of TSQM 1.4 scores between groups of patients classified by their route of medication administration: oral ($n = 357$), topical ($n = 53$), injection ($n = 53$) and inhaler ($n = 62$). Effectiveness by route $F(3552) = 11.98$, $p < 0.0001$; Side effects by route $F(3552) = 5.87$, $p < 0.001$; Convenience by route $F(3552) = 58.92$, $p < 0.0001$; Global by route $F(3552) = 4.89$, $p < 0.01$
The Treatment Satisfaction Questionnaire for Medication TSQM-II [33]	To measure patients' satisfaction with medication in chronic diseases such as coronary diseases [27], cystic fibrosis [35], hypertension [36], chronic obstructive pulmonary disease (COPD) [37], multiple sclerosis [38], diabetes [39], and autoimmune diseases such as psoriasis [40] and angiodema [41]	Adult	2– 3 weeks, or since the last medication use	11	Side effects (4 items) Effectiveness (2 items) Convenience (3 items) Global satisfaction scale (2 items)	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient:* Patients who started new medication ($n = 342$) Side effects: 0.91; Convenience: 0.91 Spearman's correlation coefficients (because these scales contain only 2 items): Effectiveness: 0.94 Overall satisfaction: 0.88

Table 1 (continued)

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Treatment Satisfaction Questionnaire for Medication TSQM-9 [34]				9	Effectiveness (3 items) Convenience (3 items) Global satisfaction scale (3 items)	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient:* Patients with hypertension and taking prescription medication for their hypertension ($n = 396$) Effectiveness: 0.935 (at day 1); 0.924 (between days 7–17) Convenience: 0.911 (at day 1); 0.915 (between days 7–17) Global satisfaction: 0.837 (at day 1); 0.848 (between days 7–17) *Test-retest reliability (reproducibility)* Patients with hypertension and taking prescription medication for their hypertension ($n = 396$) Intraclass Correlation Coefficient (ICC): Effectiveness: 0.78 Convenience: 0.74 Global satisfaction: 0.76 **Validity:** *Known-groups validity* Compliers of medication measured with the Modified Morisky Scale Low compliers (Modified Morisky Scale < 6); n= 200 Medium compliers (Modified Morisky Scale ≥6 but < 7); $n = 195$ High compliers (Modified Morisky Scale = 7); $n = 1$ *Concurrent validity* Patients with hypertension and taking prescription medication for their hypertension ($n = 396$). A correlation was found between the Modified Morisky Scale and the medication adherence domain scores (r = 0.46), the effectiveness domain scores (r = 0.38) and the global satisfaction domain scores (r = 0.34)

Table 1 (continued)

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Functional Assessment of Chronic Illness Therapy Patient Satisfaction (FACIT-TS-PS) [42]	To assess patient satisfaction with treatment for chronic illnesses such as cancer and HIV/AIDS	Adult	No information provided	29	Physician communication (12 items) Treatment staff communication (4 items) Technical competence (3 items) Nurse communication (3 items) Confidence and trust (4 items) Overall (3 items) + 1 open-ended question for comments	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient:* Physician communication ($n = 293$): 0.95 Treatment staff communication ($n = 414$): 0.89 Technical competence ($n = 49$): 0.86 Confidence and trust ($n = 58$): 0.72 Nurse communication ($n = 289$): 0.93 **Validity:** *Clinical validity* Patients with lung, breast or other types of cancer: $n = 288$ Response of FACIT-TS-PS overall item 39 "would you choose this clinic or office again ?": Yes, Maybe or No FACIT-TS-PS subscales were able to discriminate between patients according to their overall treatment satisfaction, with significantly higher mean scores observed in patients reporting higher general satisfaction Patients with lung, breast or other types of cancer: $n = 291$ Response of FACIT-TS-PS overall item 40 "How do you rate the care you received ?": Excellent, Very good, Good, or Fair FACIT-TS-PS subscales were able to discriminate between patients according to their overall treatment satisfaction, with significantly higher mean scores observed in patients reporting higher general satisfaction *Concurrent validity* Patients with various types of cancer or HIV: $n = 58$ Correlations between FACIT-TS-PS and PSQ III subscales ranged from 0.40 to 0.70, with all $p < 0.001$, except correlations of FACIT-TS-PS Nurse communication with PSQ III general (0.42; $p < 0.01$) and with PSQ III communication (0.30; $p < 0.01$)

BPH benign prostate hyperplasia, *COPD* chronic obstructive pulmonary disease, *T1DM* type 1 diabetes mellitus, *T2DM* type 2 diabetes mellitus

*Psychometric properties data sourced from ePROVIDE's PROQOLID Database [43]

Table 2 Examples of disease-specific treatment satisfaction patient-reported outcome (PRO) instruments

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Diabetes Treatment Satisfaction Questionnaire (DTSQ): Status (DTSQs) [44] and change versions (DTSQc) [45]	To measure satisfaction with diabetes treatment regimens in people with diabetes and changes in satisfaction with treatment	Adult	DTSQs: over the past few weeks DTSQc: 6 months ago (before you changed to the medication you are using now)	8	Satisfaction with treatment (6 items) Perceived hyperglycaemia (1 item) Perceived hypoglycaemia (1 item)	**Reliability:** *Internal consistency reliability: Cronbach's alpha coefficient* Insulin-dependent diabetes; $n = 128$ 0.76 (For the Satisfaction with treatment scale) Type 2 diabetes; $n = 181$ Cronbach's alpha coefficient 0.79 **Validity:** *Clinical validity* Type 2 diabetes; $n = 181$ According to the percent of ideal body weight, HbA1 levels, subjective estimates of diabetic control Greater treatment satisfaction was associated with being less overweight ($r = -0.19$; $p < 0.01$); better blood glucose control as indicated by lower HbA1 levels ($r = -0.28$; $p < 0.001$); optimistic patient estimates of recent diabetic control ($r = -0.56$; $p < 0.001$)
Cancer Therapy Satisfaction Questionnaire (CTSQ) [46, 47]	To measure satisfaction with and preference for chemotherapy treatment, and for biological therapy in either pill or intravenous administration form	Adult	In the last 4 weeks	16	Expectations of Therapy (ET): 5 items Feelings about side effects (FSE): 4 items Satisfaction with therapy (SWT): 7 items	**Reliability:** *Internal consistency reliability; Cronbach's alpha coefficients:* Oncology patients; $n = 361$ Expectations of therapy: 0.87; Feelings about side effects: 0.77; Satisfaction with therapy: 0.82; Convenience: 0.60 *Test-retest reliability (reproducibility): Intraclass correlation coefficient:* Oncology patients; $n = 53$ Expectations of therapy: 0.68; Feelings about side effects: 0.82; Satisfaction with therapy: 0.732 **Validity:** *Clinical validity* Oncology patients; $n = 361$. Cancer stage: ANOVA. ET domain ($p = 0.005$). Effect size 0.67 Stages I and IV. ECOG performance status. ET domain. Grades 0, 1, and 2 ($p = 0.0007$). Effect size 0.46 for Grades 0 vs 1. Correlation coefficient: one-way ANOVA **Ability to detect change:** *Minimal Important Difference (MID):* ET: 9.59 (0.5 SD of baseline scores); FSE 11.00 (0.5 SD of baseline scores); SWT: 6.88 (0.5 SD of baseline scores)

Table 2 (continued)

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
The Erectile Dysfunction Index of Treatment Satisfaction (EDITS) [48]	To assess satisfaction with medical treatments for erectile dysfunction	Adult	In the past 4 weeks	Patient: 11 Partner: 5	Treatment satisfaction	**Reliability:** *Internal consistency reliability* Couples with men having erectile dysfunction: $n = 28$ couples for the Patient EDITS version, and $n = 29$ couples for the Partner EDITS version *Cronbach's alpha coefficient:* 0.90 for the patients; 0.76 for the partners *Test-retest reliability (reproducibility)* Couples with men having erectile dysfunction: $n = 28$ couples for the Patient EDITS version, and $n = 29$ couples for the Partner EDITS version Spearman rank-order correlations: 0.98 for the Patient EDITS and 0.83 for the Partner EDITS

Table 2 (continued)

Name	Objective	Population	Recall period	Items	Domains	Psychometric properties*
Pain Treatment Satisfaction Scale (PTSS) [48]	To measure patient satisfaction for patients receiving treatment for either acute or chronic pain	Adult	Present time, last week or last 24 hours	39 + 22 not scored	Information (5 items) Medical care (8 items) Impact of current pain medication (8 items) Satisfaction with pain medication (2 subscales: medication characteristics [3 items] + efficacy [3 items]) Side effects (12 items) + general health items (6 items) and stand-alone questions (not scored—providing complementary information)	**Reliability:** *Internal consistency reliability:* Cronbach's alpha coefficient: Patients with acute pain ($n = 111$) and chronic pain ($n = 89$), $n = 208$ Satisfaction with current pain medication: 0.90; Efficacy subscale: 0.90; Medication characteristics subscale: 0.85; Side effects of medication: 0.83; Impact of current pain medication: 0.92; Medical care: 0.86; Information about pain and its treatment: 0.89 *Test-retest reliability (reproducibility)* a) Intraclass Correlation Coefficient (ICC) Satisfaction with current pain medication: 0.974; Efficacy subscale: 0.76; Medication characteristics subscale: 0.55; Side effects of medication: 0.67; Impact of current pain medication: 0.68; Medical care: 0.81; Information about pain and its treatment: 0.76 b) Wilcoxon signed rank test Patients with chronic pain; $n = 87$. All dimensions except information, mean scores were not significantly different between baseline and week 2; $p > 0.05$ **Validity:** *Clinical validity* Patients with acute pain ($n = 111$) and chronic pain ($n = 89$), $n = 208$. Spearman's correlation coefficient Satisfaction with current pain medication: −0.48; Efficacy subscale: −0.53; Medication characteristics subscale: −0.35; Side effects of medication: −0.17; Impact of current pain medication: −0.25; Medical care: −0.32; Information about pain and its treatment: −0.29 *Known-groups validity* Patients with acute pain ($n = 111$) and chronic pain ($n = 89$), $n = 208$ Pain severity in the last week: Scores were significantly lower (except medical care) in patients with severe pain. Pain severity after treatment: Scores were significantly lower in all scales ($p < 0.05$) in patients with severe pain. Pain severity in the last week, in the last 24 h and right now: PTSS scores were systematically lower in patients reporting more severe pain. The differences were significant for medication characteristics and side effects **Ability to detect change:** Patients with acute pain: $n = 104$. Mean ABLE change scores differed significantly for the improved group of patients based on the change in pain ($p < 0.05$), Wilcoxon signed rank test

*Psychometric properties data sourced from ePROVIDE's PROQOLID Database [43]

Where treatment satisfaction has been measured in clinical trials, it has tended to be in the later phases of drug development. An analysis of *clinicaltrials.gov* data on the use of the Treatment Satisfaction Questionnaire for Medication (TSQM) over the 5-year period between 2016–2021 demonstrates that TSQM has been more frequently used in phase III interventional studies than in phase II or phase I trials [54]. Its use in later phase trials makes sense. Once the safety and efficacy of a drug have been explored in an early phase study, measuring domains of satisfaction helps researchers and sponsors understand why one compound, dose, or method of administration may be preferred over another, predict adherence, and support messages regarding the value of the product to patients. However, treatment satisfaction may also have an important role to play in earlier phases of drug development. Treatment satisfaction in dose finding research (phase I/II) can inform the selection of doses for later trials, especially for products used for the treatment of chronic conditions that require adherence to medication over long periods of time. In such trials, an understanding of satisfaction with treatment can offer some insight and hypotheses [24]. For example, treatment satisfaction data can evaluate medical treatment in clinical trials, contributes to quality assurance, and facilitates product differentiation [57]. Specifically, in the field of cancer clinical trials, reported levels of treatment satisfaction added a unique view for the evaluation of treatment efficacy [58].

Treatment satisfaction data is also important in post-registration (phase IIIb/IV) real-world settings because it can provide valuable insight into the economic valuations and cost-effectiveness assessments of medical products, such as whether or not a treatment is worthy of reimbursement [59]. Real-world evidence (RWE) studies involve a greater number of diverse patients and in general a more representative population [60], which can further help inform regulatory decisions, reimbursement, and health policy-making. There are several measures of treatment satisfaction that have been used in RWE studies. For example, the TSQM has been used to measure treatment satisfaction in amyotrophic lateral sclerosis [61] [62], the Treatment Satisfaction with Medicines Questionnaire (SATMED-Q) in acromegalia patients [63], the Diabetes Treatment Satisfaction Questionnaire (DTSQ) in patients with type 2 diabetes [64], and the Cancer Therapy Satisfaction Questionnaire (CTSQ) in metastatic squamous cell carcinoma of the head and neck [65].

Patient-centered drug development is a shift in the way that drugs are developed, involving patients in all phases of drug development. In patient-centered research, patients are considered co-researchers informing the decisions about unmet needs, trial endpoints, trial design, and execution. Drug development companies that incorporate patient voice through treatment satisfaction PRO instruments are more likely to ensure a fit of their product to the patients' needs in routine practice and provide the benefits patients are seeking. Specifically, treatment satisfaction measures allow for treatment comparison in clinical trials or the identification of the need to switch a patient's treatment in clinical practice. Additionally, these measures can address, among other outcomes, the willingness of patients to accept the negative effects of their treatment, adherence to the prescribed medication, and can be related to the overall effectiveness of their treatment [23]. Therefore, we highly recommend assessing treatment satisfaction in the different stages of drug development: during the initial development and validation, as well as at the point of implementation and communication of the results. Furthermore, it is more probable that this data can be proactively utilized to aid in regulatory decision making.

5 Treatment Satisfaction in Regulatory Decision Making

The regulatory environment is primed to consider data on treatment satisfaction from drug development. Both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have noted the critical importance of involving patients in the identification of health priorities and the outcomes desired from health interventions and in understanding the patient experience with these interventions [66]. Data from reliable, valid, and responsive PRO instruments can be considered as 'fit for purpose' and help regulators make approval decisions [49–51].

The EMA has a long history of working with patients and patient data. In 2005, a reflection paper was developed as a framework for interaction between EMA and patients, consumers, and consumer organizations to encourage the collection of PRO data [67]. In EMA's 'Regulatory Science Strategy to 2025,' one core recommendation is to "ensure the patient voice is incorporated all along the regulatory lifecycle of a medicine", reflecting the importance the Agency places on such engagement [67]. The FDA also has a long history of patient engagement, starting from 1988 with the formation of an office to work with patient advocates [66]. In 2009, the FDA developed the PRO Guidance that outlines the rigor used by regulators to review and evaluate existing, modified, or newly developed PRO instruments to support label claims [68]. More recently, the FDA launched its PFDD initiative as a commitment to capture and submit patient experience data and other relevant information from patients for drug development and regulatory decision making more systematically [20].

At the FDA and EMA, evidence supporting efficacy and safety of the medication being developed is included in the 'label' at the point of approval (FDA 'label' is the US Prescribing Information; EMA label is the Summary of Product Characteristics). The primary purpose of drug labeling is to

give healthcare professionals the information they need to prescribe the medicine appropriately [69]. The label cannot include promotional, false, or misleading statements [69]. It can, however, include other information deemed to be relevant and important in understanding the medication, assuming that the data is derived from fit-for-purpose measurement in adequate and well-controlled clinical investigations. The EMA considers both single and multidimensional domains—such as health status and satisfaction with treatment—for inclusion in labelling [70]. While traditionally more focused on core signs and symptoms of disease, recent PFDD guidance and workshop discussion from FDA proposes satisfaction as one component of a benefit–risk appraisal [20] [71].

Data extracted from 2010 until 2023 indicates that 57 drugs or medical products have included treatment satisfaction claims in their label, all using PRO instruments [43]. The EMA has approved 19 drugs (33.3%) and 38 (66.6%) have been approved by the FDA. Various PRO instruments have been used to support these claims, including the aforementioned TSQM which meets the evidence needed by regulators to support label decisions in certain contexts of use [57]. The TSQM supported six of the aforementioned treatment satisfaction label claims (5/19 drugs the EMA approved with treatment satisfaction claims in their label and 1/38 drugs the FDA approved with treatment satisfaction claims in their label) [72–77]. However, this represents only a small fraction of drugs approved in this timescale.

Therefore, treatment satisfaction is appealing to agencies because of its utility as a well-known patient-reported endpoint that captures patient experience [54, 57]. The assessment of treatment satisfaction plays an increasingly important role in regulatory decision making which ultimately improves the quality and value of health care [78] [79].

6 Treatment Satisfaction in Health Technology Assessment (HTA)

HTA agencies play a vital role in assessing the safety, efficacy, cost, and benefits of new treatments [80], which requires consideration of the patient experience with the given treatment. Patients are going to be the first beneficiaries of health innovation and are best suited to evaluate treatment satisfaction. Therefore, some HTA agencies have been utilizing PRO instruments to capture the patient's voice when evaluating pharmacotherapies or medical technologies.

PRO instruments are a key component of decision making during the benefit–risk appraisal of new drugs or biologic products across different therapeutic areas [81]. Data from reliable, valid, and responsive (i.e., 'fit for purpose') PRO instruments can help HTA bodies make access decisions [49–51]. For example, when assessing the effectiveness of a drug, not only are the clinical outcomes significant to regulatory and reimbursement agencies, but also the drug's influence on patients' daily lives, functional status, treatment satisfaction, preferences, and adherence [82]. The inclusion of treatment satisfaction measures is an effective way to assess and evaluate patient experience with the new treatment by HTA agencies. For example, treatment satisfaction measures can help HTA bodies choose between two treatments that have similar biomedical effects but present differences in terms of side effects, convenience, and mode of administration. Moreover, HTAs look for evidence to help inform formulary decisions, both at launch and during post-launch reviews. They may find that treatment satisfaction data can support and complement the traditional efficacy and safety data available from classical clinical endpoints [82]. However, there are substantial differences in HTA reimbursement decisions that could be explained by the different processes and policies in place at different HTA agencies, such as criteria for the extent of added value versus cost effectiveness [83]. Such discrepancies across countries make it challenging for sponsors not only to identify and utilize appropriate PRO instruments to capture the patient experience but also to develop appropriate methodologies for capturing these data within both clinical trial and real-world settings. However, HTA bodies have recognized treatment satisfaction can confirm clinical benefits and support reimbursement recommendations, and thus it is essential to continue to include treatment satisfaction as a key assessment throughout the drug development and commercialization process.

7 A Call to Action

Patients are in a unique position to provide treatment satisfaction assessment as they are the ones who experience the effectiveness and side effects of the therapy. Several PRO instruments offer robust fit-for-purpose (reliable, valid, sensitive) measurement of treatment satisfaction, and research has shown these can predict the likelihood of patients continuing to use their medication, the correct usage of the medication, and adherence to the treatment. It is also known that treatment satisfaction can support drug development and needs to be considered by most of the stakeholders involved in the healthcare system, from development to launch of a product and within routine clinical practice use. Moreover, the FDA and EMA have approved treatment satisfaction in label claims of certain medications. Measuring treatment satisfaction more frequently in clinical trials and studies will give us a comprehensive understanding of patient health status, facilitating appropriate and optimal treatment decisions and improving future drug development.

We encourage measuring treatment satisfaction across the phases of interventional studies and RWE studies as doing

so can be beneficial for the different stakeholders involved in drug development and regulatory decision making: (1) for pharmaceutical companies, satisfaction with a specific type of medication should lead to a differential advantage in the marketplace, product success, manufacturer profitability, and better market access; (2) for healthcare systems, understanding patient satisfaction is a critical pillar to develop more efficient and effective care models; (3) for patients, higher treatment satisfaction can lead to increased treatment adherence and better clinical outcomes.

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Declarations

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